

**AMENDMENTS TO THE CLAIMS**

**This listing of claims will replace all prior versions and listings of claims in the application:**

**LISTING OF CLAIMS:**

1. (original) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding fragment thereof, and wherein said antibody or said fragment specifically binds to insulin-like growth factor-I receptor, selected from the group consisting of:

(i) an antibody, or epitope-binding fragment thereof, having the same amino acid sequence as the murine antibody EM164 produced by mouse hybridoma EM164 (ATCC accession number PTA-4457),

(ii) a resurfaced antibody, or epitope-binding fragment thereof, having the same binding specificity as murine antibody EM164,

(iii) a human or humanized antibody, or epitope-binding fragment thereof, having the same binding specificity as murine antibody EM164,

(iv) a functional equivalent of an antibody, or epitope-binding fragment thereof, having the same binding specificity as murine antibody EM164,

(v) a variant of murine antibody EM164, or epitope-binding fragment thereof, having at least one nucleotide mutation, deletion or insertion compared to murine antibody EM164, and having the same binding specificity as murine antibody EM164, and

(vi) the murine antibody EM164 produced by mouse hybridoma EM164 (ATCC accession number PTA-4457), or epitope-binding fragment thereof, and

(b) a second therapeutic agent.

2. (currently amended) The composition according to claim 1, wherein said second therapeutic agent is selected from the group consisting of docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab (Herceptin), capecitabine, tamoxifen, toremifene, letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab (Avastin), 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab (Rituxan), idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab (Zevalin), tositumomab (Bexxar), interferon alpha-2b, melphalam, bortezomib (Velcade), altretamine, asparaginase, gefitinib (Iressa), erlonitib (Tarceva), anti-EGF receptor antibody (Cetuximab, Abx-EGF), thalidomide, carmustine, prednisone, interferon alpha-2a, vincristine, pamidronate, erythropoietin, bisphosphonate and an epothilone.

3. (original) The composition according to claim 1, wherein said second therapeutic agent is selected from the group consisting of carboplatin, oxaliplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, and camptothecin.

4. (original) The composition according to claim 1, wherein said first therapeutic agent is administered to patient at a dosage of about 1 mg/square meter to about 2000 mg/square meter, and wherein said second therapeutic agent is administered at a dosage of about 10 mg/square meter to about 2000 mg/square meter.

5. (original) The composition according to claim 1, wherein said first therapeutic agent is administered to patient at a dosage of about 10 mg/square meter to about 1000 mg/square meter, and wherein said second therapeutic agent is administered at a dosage of about 50 mg/square meter to about 1000 mg/square meter.

6. (original) A pharmaceutical composition comprising the composition according to claim 1, and a pharmaceutically acceptable carrier or diluent.

7. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding antibody fragment comprising at least one complementarity-determining region having an amino acid sequence selected from the group consisting of:

SYWMH (SEQ ID NO:1),  
EINPSNGRTNYNEKFKR (SEQ ID NO:2),  
GRPDYYGSSKWYFDV (SEQ ID NO:3),  
RSSQSIVHSNVNTYLE (SEQ ID NO:4),  
KVSNRFS (SEQ ID NO:5), and  
FQGSHPPT (SEQ ID NO:6), and

(b) a second therapeutic agent, wherein when SEQ ID NO:5 is selected said antibody or antibody fragment specifically binds to insulin-like growth factor-I receptor.

8. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding antibody fragment comprising at least one heavy chain variable region and at least one light chain variable region, wherein said heavy chain variable region comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS:1-3, respectively:

SYWMH (SEQ ID NO:1),  
EINPSNGRTNYNEKFKR (SEQ ID NO:2),  
GRPDYYGSSKWYFDV (SEQ ID NO:3);

and wherein said light chain variable region comprises three sequential complementarity-determining regions having amino acid sequences represented by SEQ ID NOS:4-6, respectively:

RSSQSIVHSNVNTYLE (SEQ ID NO:4),  
KVSNRFS (SEQ ID NO:5),

FQGSHPPT (SEQ ID NO:6), and

(b) a second therapeutic agent.

9. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding fragment thereof wherein said antibody or said fragment comprises a heavy chain variable region that has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:7:

QVQLQQSGAELVKPGASVKLSCKASGYTFTSYWMHWVKQRPGQGLEWIGEINPSNGR  
TNYNEKFKRKATLTVDKSSSTAYMQLSSLTSEDSAVYYFARGRPDYYGSSKWYFDVW  
GAGTTVTVSS (SEQ ID NO:7), and

(b) a second therapeutic agent.

10. (previously presented) The composition of claim 9, wherein said heavy chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:7.

11. (previously presented) The composition of claim 9, wherein said heavy chain variable region has an amino acid sequence that is represented by SEQ ID NO:7.

12. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding fragment thereof wherein said antibody or said fragment comprises a light chain variable region that has at least 90% sequence identity to an amino acid sequence represented by SEQ ID NO:8:

DVLMTQTPLSLPVSLGDQASISCRSSQSIVHSNVTYLEWYLQKPGQSPKLLIYK  
VSNRFSGVPDRFSGSGGTDFTLRISRVEAEDLGIYYCFQGSHPPTFGGGTKLEIKR  
(SEQ ID NO:8), and

(b) a second therapeutic agent.

13. (previously presented) The composition of claim 12, wherein said light chain variable region has at least 95% sequence identity to said amino acid sequence represented by SEQ ID NO:8.

14. (previously presented) The composition of claim 12, wherein said light chain variable region has an amino acid sequence that is represented by SEQ ID NO:8.

15. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding fragment thereof wherein said antibody or said fragment comprises a light chain variable region having a sequence selected from the group consisting of:

DVVMQTQTPLSLPVSLGDPASISCRSSQSIVHSNVNTYLEWYLQKPGQSPRLLIYKV  
SNRFSGVPDRFSGSGAGTDFTLRISRVEAEDLGIYYCFQGSHVPPTFGGGGTKLEIKR  
(SEQ ID NO:9);

DVLMTQTPLSLPVSLGDPASISCRSSQSIVHSNVNTYLEWYLQKPGQSPKLLIYKV  
SNRFSGVPDRFSGSGAGTDFTLRISRVEAEDLGIYYCFQGSHVPPTFGGGGTKLEIKR  
(SEQ ID NO:10);

DVLMTQTPLSLPVSLGDPASISCRSSQSIVHSNVNTYLEWYLQKPGQSPRLLIYKV  
SNRFSGVPDRFSGSGAGTDFTLRISRVEAEDLGIYYCFQGSHVPPTFGGGGTKLEIKR  
(SEQ ID NO:11);

DVVMQTQTPLSLPVSLGDPASISCRSSQSIVHSNVNTYLEWYLQKPGQSPKLLIYK  
VSNRFSGVPDRFSGSGAGTDFTLRISRVEAEDLGIYYCFQGSHVPPTFGGGGTKLEIKR  
(SEQ ID NO:12), and

(b) a second therapeutic agent.

16. (previously presented) A composition comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody or an epitope-binding fragment thereof wherein said antibody or said fragment comprises a heavy chain variable region having a sequence represented by SEQ ID NO:13:

QVQLVQSGAEVVKPGASVKLSCKASGYTFTSYWMHWVKQRPGQGLEWIGEINP  
SNGRTNYNQKFQGKATLTVDKSSSTAYMQLSSLTSEDSAVYYFARGRPDYYGSSKWYF  
DVWGQGTTVTVSS (SEQ ID NO:13), and

(b) a second therapeutic agent.

17. (currently amended) The composition of any one of claims 7-16, wherein said second therapeutic agent is selected from the group consisting of docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab (Herceptin), capecitabine, tamoxifen, toremifene, letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab (Avastin), 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab (Rituxan), idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab (Zevalin), tositumomab (Bexxar), interferon alpha-2b, melphalam, bortezomib (Velcade), altretamine, asparaginase, gefitinib (Iressa), erlonitib (Tarceva), anti-EGF receptor antibody (Cetuximab, Abx-EGF), thalidomide, carmustine, prednisone, interferon alpha-2a, vincristine, pamidronate, erythropoietin, bisphosphonate and an epothilone.

18. (original) The composition of any one of claims 7-16, wherein said second therapeutic agent is selected from the group consisting of carboplatin, oxaliplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, and camptothecin.

19. (original) A method for inhibiting the growth of a cancer cell comprising contacting said cell with the composition of claim 1.

20. (original) A method for treating a patient having a cancer comprising administering to said patient an effective amount of the composition of claim 1.

21. (original) A method for treating a patient having a cancer comprising administering to said patient an effective amount of the pharmaceutical composition of claim 6.

22. (original) The method of treatment of any one of claims 19-21, wherein said cancer is a cancer selected from the group consisting of breast cancer, colon cancer, ovarian carcinoma, osteosarcoma, cervical cancer, prostate cancer, lung cancer, synovial carcinoma, pancreatic cancer, melanoma, multiple myeloma, neuroblastoma, and rhabdomyosarcoma.

23. (original) A kit comprising:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody having the same amino acid sequence as the murine antibody EM164 produced by mouse hybridoma EM164 (ATCC accession number PTA-4457), or an epitope-binding fragment thereof, wherein said antibody or said fragment specifically bind to insulin-like growth factor-I receptor,

(b) a second therapeutic agent, and

(c) instructions for use.

24. (original) A method for inhibiting the growth of a cancer cell comprising contacting said cell with:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody having the same amino acid sequence as the murine antibody EM164 produced by mouse hybridoma EM164 (ATCC accession number PTA-4457), or an epitope-binding fragment thereof, wherein said antibody or said fragment specifically bind to insulin-like growth factor-I receptor, and

(b) a second therapeutic agent.

25. (original) A method for treating a patient having a cancer comprising administering to said patient an effective amount of:

(a) a first therapeutic agent, wherein said first therapeutic agent is an antibody having the same amino acid sequence as the murine antibody EM164 produced by mouse hybridoma EM164 (ATCC accession number PTA-4457), or an epitope-binding fragment thereof, wherein said antibody or said fragment specifically bind to insulin-like growth factor-I receptor, and

(b) a second therapeutic agent.

26. (original) The method of claim 24, wherein said cell is contacted with said first therapeutic agent and said second therapeutic agent concurrently.

27. (original) The method of claim 24, wherein said cell is contacted with said first therapeutic agent and said second therapeutic agent sequentially and in either order.

28. (original) The method of claim 25, wherein said first therapeutic agent and said second therapeutic agent are administered concurrently.

29. (original) The method of claim 25, wherein said first therapeutic agent and said second therapeutic agent are administered sequentially and in either order.

30. (currently amended) The method of claim 24 or 25, wherein said second therapeutic agent is selected from the group consisting of docetaxel, paclitaxel, doxorubicin, epirubicin, cyclophosphamide, trastuzumab (Herceptin), capecitabine, tamoxifen, toremifene, letrozole, anastrozole, fulvestrant, exemestane, goserelin, oxaliplatin, carboplatin, cisplatin, dexamethasone, antide, bevacizumab (Avastin), 5-fluorouracil, leucovorin, levamisole, irinotecan, etoposide, topotecan, gemcitabine, vinorelbine, estramustine, mitoxantrone, abarelix, zoledronate, streptozocin, rituximab (Rituxan), idarubicin, busulfan, chlorambucil, fludarabine, imatinib, cytarabine, ibritumomab (Zevalin), tositumomab (Bexxar), interferon alpha-2b, melphalam, bortezomib (Velcade), altretamine, asparaginase, gefitinib (Iressa), erlonitib (Tarceva), anti-EGF receptor antibody (Cetuximab, Abx-EGF), thalidomide, carmustine, prednisone, interferon alpha-2a, vincristine, pamidronate, erythropoietin, bisphosphonate and an epothilone.

31. (original) The method of claim 24 or 25, wherein said second therapeutic agent is selected from the group consisting of carboplatin, oxaliplatin, cisplatin, paclitaxel, docetaxel, gemcitabine, and camptothecin.

32. (new) The method of claim 1, wherein said second therapeutic agent is selected from the group consisting of bortezomib (Velcade), melphalan, thalidomide, doxorubicin,



cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.

33. (new) The composition of any one of claims 7-16, wherein said second therapeutic agent is selected from the group consisting of bortezomib (Velcade), melphalan, thalidomide, doxorubicin, cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.

34. (new) The method of claim 24 or 25, wherein said second therapeutic agent is selected from the group consisting of bortezomib (Velcade), melphalan, thalidomide, doxorubicin, cyclophosphamide, interferon alpha-2b, interferon alpha-2a, vincristine, pamidronate, carmustine, prednisone, zoledronate, erythropoietin, bisphosphonate and dexamethasone.